U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

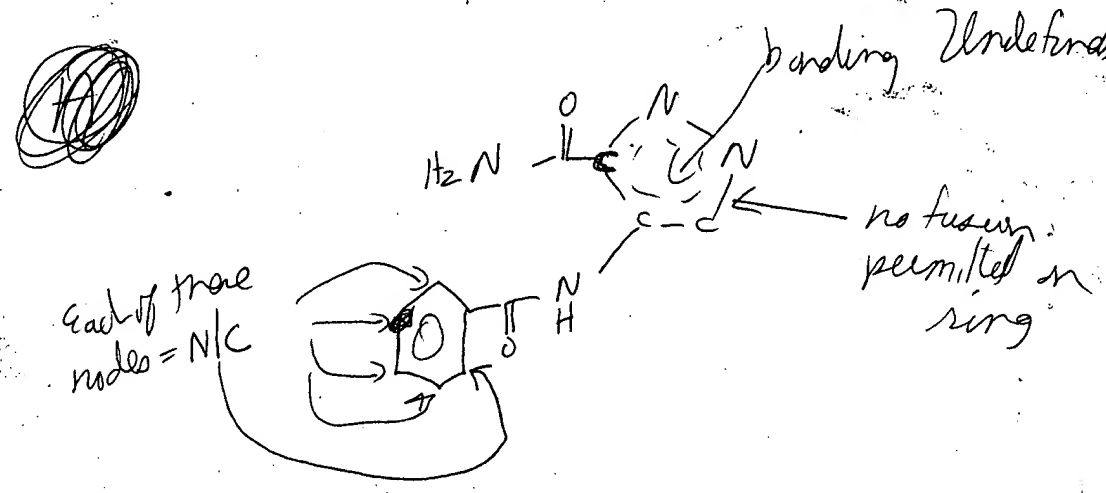
SEARCH REQUEST FORM 59330

Requestor's Name: BERCH Serial Number: 09/916099

Date: 1/30/02 Phone: ~~4D15~~ 4718 (4D15 4E12) Art Unit: 1624

Search Topic: meg

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).



I need Biblios only (no structures)

RECEIVED JAN 30 2002 (1600)

1116
1110

MARY

STAFF USE ONLY

Date completed: 2/1
Searcher: Mary
Terminal time:
Elapsed time:
CPU time:
Total time: 6
Number of Searches:
Number of Databases:

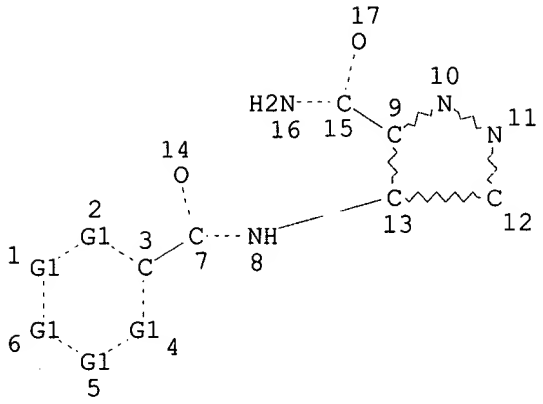
Search Site
- STIC
- CM-1
- Pre-S

Type of Search
- N.A. Sequence
- A.A. Sequence
- 1 Structure
- Bibliographic

Vendors
- IC Suite
- 254.7 STN
- Dialog
- APS
- Geninfo
- SDC
- DARC/Questel
- Other

Beach
916099

=> d l3 que stat;fil medl,caplus,biosis,embase,jicst;s l3
L1 STR



VAR G1=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 9
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L3 204 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 224 ITERATIONS 204 ANSWERS
SEARCH TIME: 00.00.02

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	141.18	141.33

FILE 'MEDLINE' ENTERED AT 11:15:16 ON 01 FEB 2002

FILE 'CAPLUS' ENTERED AT 11:15:16 ON 01 FEB 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 11:15:16 ON 01 FEB 2002

FILE 'EMBASE' ENTERED AT 11:15:16 ON 01 FEB 2002

FILE 'JICST-EPLUS' ENTERED AT 11:15:16 ON 01 FEB 2002

L4 0 FILE MEDLINE
L5 41 FILE CAPLUS
L6 0 FILE BIOSIS
L7 0 FILE EMBASE
L8 0 FILE JICST-EPLUS

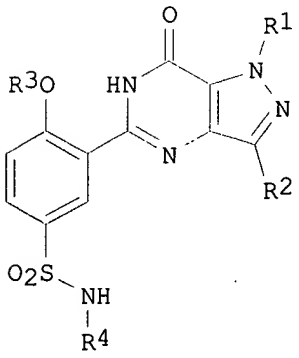
Searched by: Mary Hale 308-4258 CM-1 12D16

TOTAL FOR ALL FILES
L9 41 L3

=> d 1-41 cbib abs

L9 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:935607 Document No. 136:53762 A process for preparing pyrazolopyrimidinone derivatives for the treatment of impotence. Yoo, Moo-Hi; Kim, Won-Bae; Chang, Min-Sun; Kim, Soon-Hoe; Kim, Dong-Sung; Bae, Chul-Jun; Kim, Yong-Duck; Kim, Eun-Ha (Dong A Pharm. Co., Ltd., S. Korea). PCT Int. Appl. WO 2001098304 A1 20011227, 32 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-KR819 20010518. PRIORITY: KR 2000-34966 20000623.

GI



I

AB The title compds. [I; R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl, cycloalkyl, etc.; R3 = alkyl, cycloalkyl, alkenyl, etc.; R4 = alkyl, alkenyl, cycloalkyl, etc.] having efficacy on the treatment of impotence, one of male sexual dysfunctions (no data given), were prepd. in high yield and in an economic manner. The method according to the present invention comprises the steps of chlorosufonation the pyrazolamide, followed by amination with amine and intramol. cyclization. Thus, chlorosulfonation of 4-(2-propoxybenzamido)-1-methyl-3-propyl-5-carbamoylpyrazole (prepn. given) followed by amination of the resulting intermediate with 2-(2-aminoethyl)-1-methylpyrrolidine, and cyclization of 4-{2-propoxy-5-[2-(1-methyl-2-pyrrolidinyl)ethylamidosulfonyl]benzamido}-1-methyl-3-propyl-5-carbamoylpyrazole afforded I [R1 = Me; R2 = Pr; R3 = Pr; R4 = 2-(1-methyl-2-pyrrolidinyl)ethyl].

L9 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:935606 Document No. 136:53761 Novel process for the preparation of pyrazolopyrimidinones. Bunnage, Mark Edward; Levett, Philip Charles; Thomson, Nicholas Murray (Pfizer Limited, UK; Pfizer Inc.). PCT Int. Appl. WO 2001098303 A1 20011227, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,

MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-IB1038 20010607. PRIORITY: GB 2000-15462 20000622; GB 2001-5878 20010309.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

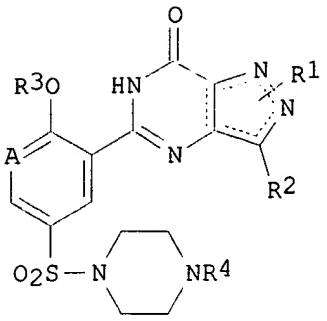
AB A process for the prodn. of a compd. of general formula I [A = CH, N; R1 = lower alkyl (optionally interrupted by oxygen), Het, alkylHet, aryl, alkylaryl, etc. (Het = (un)substituted four to twelve-membered heterocyclic group which contains one or more heteroatoms selected from N, O, and S); R2, R4 = independentally lower alkyl; R3 = lower alkyl (optionally interrupted by oxygen)], which process comprises the dehydrogenation of a compd. of general formula II. Thus, 4-{6-ethoxy-5-[3-ethyl-6,7-dihydro-7-oxo-2-(2-pyridylmethyl)-2H-pyrazolo[4,3-b]pyrimidin-5-yl]3-pyridinylsulfonyl}-1-ethylpiperizine (III) was produced from 4-{6-ethoxy-5-[3-ethyl-4,5,6,7-tetrahydro-7-oxo-2-(2-pyridylmethyl)-2H-pyrazolo[4,3-b]pyrimidin-5-yl]3-pyridinylsulfonyl}-1-ethylpiperizine (IV) via dehydrogenation in 84% yield.

L9 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2002 ACS

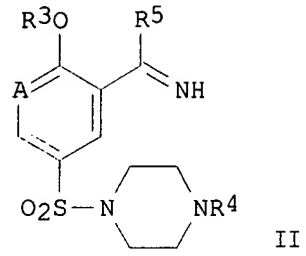
2001:935589 Document No. 136:69817 Process for the preparation of pyrazolopyrimidinones (e.g. Sildenafil) by cyclocondensation of benzimidates with aminopyrazolecarboxamides.. Dunn, Peter James; Dunne, Catherine (Pfizer Limited, UK; Pfizer Inc.). PCT Int. Appl. WO 2001098284 A1 20011227, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-IB1050 20010611. PRIORITY: GB 2000-15472 20000622; GB 2001-5857 20010309.

GI

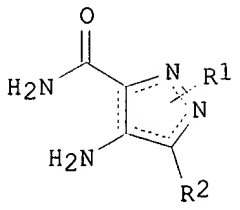
Searched by: Mary Hale 308-4258 CM-1 12D16



I



II



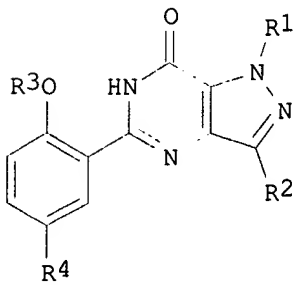
III

AB Title compds. [I; A = CH , N; R1 = H, (substituted) alkyl (optionally interrupted by O), Het, alkylHet, aryl, alkylaryl; R2, R4 = alkyl; R3 = (O-interrupted) alkyl; Het = (substituted) 4- to 12-membered heterocyclyl contg. .gtoreq.1 of N, O, S], were prepd. by reaction of imidates (II; R5 = group substitutable by aminopyrazole; other variables as above) with aminopyrazolecarboxamides (III; variables as above). Thus, Et 2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl)benzimidate (prepn. given), 4-amino-1-methyl-3-propyl-1H-pyrazole-5-carboxamide were refluxed in xylene/EtOAc to give 76% sildenafil.

L9 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2002 ACS

2001:851163 Document No. 136:6002 Preparation of pyrazolopyrimidinones as PDE V inhibitors. Kim, Dae-Kee; Lee, Ju Young; Lee, Nam Kyu; Ryu, Do Hyun; Kim, Jae-Sun; Choi, Jin Young; Lee, Suk Ho; Im, Guang-Jin; Cha, Hoon; Kim, Tae Kon; Kim, Key Hyup (SK Chemicals Co., Ltd., S. Korea). PCT Int. Appl. WO 2001087888 A1 20011122, 100 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-KR480 20000517.

GI



I

Searched by: Mary Hale 308-4258 CM-1 12D16

AB The title compds. [I; R1 = H, alkyl optionally substituted with one or more fluoro atoms, cycloalkyl; R2 = H, (un)substituted alkyl, cycloalkyl, etc.; R3 = alkyl optionally substituted with cycloalkyl or with one or more F atoms, alkenyl, cycloalkyl, etc.; R4 = SO2NR5R6, NHCOR7; R5 and R6 together with the N atom to which they are attached form (un)substituted pyrrolidinyl, piperidino, morpholino or piperazino; R7 = alkyl optionally substituted with cycloalkyl or with one or more F atoms, cycloalkyl] having an excellent inhibiting activity against cyclic guanosine 3',5'-monophosphate specific phosphodiesterase (cGMP specific PDE; PDE V), were prepd. Thus, cyclization of 4-{5-[4-(hydroxycarbonyl)piperidinylsulfonyl]-2-propoxybenzamido}-1-methyl-3-propylpyrazole-5-carboxamide (prepn. given) in the presence of aq. 1N NaOH in EtOH afforded 91% I [R1 = Me; R2, R3 = Pr; R4 = 4-(hydroxycarbonyl)piperidinylsulfonyl] which showed an excellent inhibitory activity against PDE V with IC50 of 0.02-0.5 nM.

L9 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:796237 Document No. 135:344497 Synthesis and use of pyrazolo-pyrimidines as estrogen agonists/antagonists for treating female sexual dysfunction. Lee, Andrew George; Thompson, David Duane; Day, Wesley Warren (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1149579 A2 20011031, 47 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2001-303481 20010412. PRIORITY: US 2000-PV266387 20000418.
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A = CH2, NR; X, D, E = CH, N; Y = Ph, naphthyl, cycloalk(en)yl, heterocyclyl, etc.; Z1 = alkyl, alkyloxy, alkylamino, etc.; G = amino; R = H, alkyl; n = 0 - 2] were prepd. For example, 4-amino-3-ethyl-1H-pyrazole-5-carboxamide was condensed with 3-carboxy-2-ethoxy-5-(4-ethylpiperazin-1-ylsulfonyl)pyridine (prepn. given, DMF, HOBt, Et3N, EDCI, room temp., 6 h). The pyrazole moiety of the resulting adduct was N-alkylated (DMF, Cs2CO3, Br(CH2)2OMe, 60.degree.C, 18 h) and cyclized to pyrazolo[4,3-d]pyrimidine II (EtOH, EtOAc, KHMDS, 120.degree.C, 12 h). I are estrogen receptor agonists/antagonists and when co-administered with a cyclic 3',5'-guanosine monophosphate elevator, are used to treat (e.g.) hypoactive sexual desire disorder, sexual arousal disorder, etc.

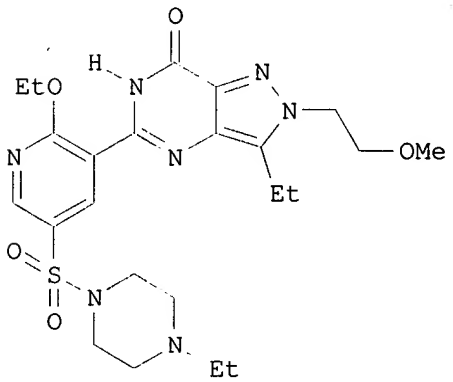
L9 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:711627 Synthesis and vasorelaxant potency of monagra. A chiral 5-(2-methyl-2,3-dihydro-7-benzofuryl)pyrazolopyrimidone analog of Viagra. Al-Bojuk, Nader R.; El-Abadelah, Mustafa M.; Sabri, Salim S.; Michel, Alain; Voelter, Wolfgang; M.-Mossmer, Cacilia; Al-Abed, Yousef (Chemistry Department, Faculty of Science, Jordan University, Amman, Jordan). Heterocycles, 55(9), 1789-1803 (English) 2001. CODEN: HTCYAM. ISSN: 0385-5414. Publisher: Japan Institute of Heterocyclic Chemistry.
AB Synthesis and properties of a chiral 5-(2-methyl-2,3-dihydro-7-benzofuryl)pyrazolo[4,3-d]pyrimidin-7-one (I), an analog of Viagra and Biagra, are described. The key material, (.+-.)-3-methyl-2,3-dihydrobenzofuran-7-carboxylic acid was resolved into the (S)- (95% ee) and (R)- (99% ee) enantiomers using, resp., (-)-cinchonidine and (+)-cinchonine. The abs. configuration of this R-enantiomer was detd. as R by x-ray measurements [monoclinic, P21, a 7.4840(5), b 9.3550(7), c 12.7760(7).ANG., .alpha. 90, .beta. 105.502(5), .gamma. 90.degree., V

Searched by: Mary Hale 308-4258 CM-1 12D16

861.94(10) .ANG.3, Z 2]. Preliminary in vitro expts. on rat isolated thoracic aorta show that the vasorelaxant potency of R-I and S-I is truly higher than that of Viagra and Biagra.

L9 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:652871 Document No. 135:180785 Intramolecular cyclocondensation process for the preparation of 1-[[3-(4,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methylpiperazine. Lu, Yee-Fung; Antczak, Casimir; Tao, Yong; Oudenes, Jan (Torcan Chemical Ltd., Can.). Braz. Pedido PI BR 9803911 A 20000328, 21 pp. (Portuguese). CODEN: BPXXDX. APPLICATION: BR 1998-3911 19980902. PRIORITY: AR 1998-102272 19980515.
AB A cyclocondensation process for the prepn. of 1-[[3-(4,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methylpiperazine, sildenafil, is presented.

L9 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:615491 Document No. 135:180782 Use of estrogen agonists/antagonists for the treatment of sexual dysfunction. Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1125582 A2 20010822, 45 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2001-300061 20010105. PRIORITY: US 2000-PV175704 20000112.
GI



I

AB Pyridinylpyrazolopyrimidinone cGMP PDEv inhibitors, e.g., I were prepd. Data for biol. activity of 3-[1-[4-(2-dimethylaminoethoxy)phenyl]-2-phenyl-1-butenyl]phenol were given.

L9 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:466998 Document No. 135:257117 Synthesis and phosphodiesterase 5 inhibitory activity of new 5-phenyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one derivatives containing an N-acylamido group on a phenyl ring. Kim, D.-K.; Ryu, D. H.; Lee, N.; Lee, J. Y.; Kim, J.-S.; Lee, S.; Choi, J.-Y.; Ryu, J.-H.; Kim, N.-H.; Im, G.-J.; Choi, W.-S.; Kim, T.-K. (Life Science Research Center, SK Chemicals, Suwon-Si, Changan-Ku, Kyungki-Do, 440-745, S. Korea). Bioorganic & Medicinal Chemistry, 9(7), 1895-1899 (English) 2001. CODEN: BMECEP. ISSN: 0968-0896. Publisher: Elsevier Science Ltd..
AB New sildenafil analogs with an N-acylamido group at the 5'-position of the Ph ring were prepd. from the readily available starting compd. in four straightforward steps. Enzyme assays demonstrated that all the target compds. showed higher PDE5 inhibitory activities than sildenafil. It was

obsd. that the PDE5 inhibitory activity was enhanced as the chain length of the R group increased, but introduction of the branched alkyl groups such as iso-Pr and cyclohexyl resulted in a drop of potency. In particular the N-butyrylamido deriv. exhibited the highest PDE5 inhibitory activity, and was about 6-fold more potent than sildenafil. However, all the compds. exhibited somewhat weak selectivity (1-3-fold) over PDE6.

L9 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2002 ACS

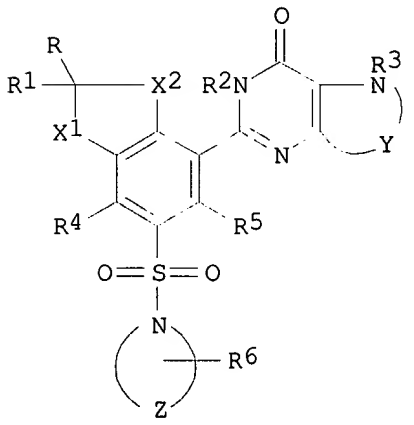
2001:426036 Document No. 135:282669 Synthesis and phosphodiesterase 5 inhibitory activity of novel phenyl ring modified sildenafil analogues. Kim, D.-K.; Lee, N.; Lee, J. Y.; Ryu, D. H.; Kim, J.-S.; Lee, S.-H.; Choi, J.-Y.; Chang, K.; Kim, Y.-W.; Im, G.-J.; Choi, W.-S.; Kim, T.-K.; Ryu, J.-H.; Kim, N.-H.; Lee, K. (SK Chemicals, Life Science Research Center, Changan-Ku, Suwon-Si, Kyungki-Do, 440-745, S. Korea). Bioorganic & Medicinal Chemistry, 9(6), 1609-1616 (English) 2001. CODEN: BMECEP. ISSN: 0968-0896. Publisher: Elsevier Science Ltd..

AB New sildenafil analogs contg. an ether ring fused into the Ph moiety were efficiently synthesized from readily available starting materials in five steps. Ab initio calcns. indicated that introduction of a cyclic ether to the Ph group might enhance the co-planarity of the mol. The in vitro PDE 5 inhibitory activity was found out to be inversely related to the degree of co-planarity. In other words, the least planar sildenafil showed the highest activity, and the most planar 5-membered cyclic ether derivs. were least active by 100-200-fold compared with sildenafil. Our study clearly demonstrated that the open chain 2'-alkoxy group of the Ph ring, although less effective for inducing the co-planarity, seemed to act as a much better lipophilic requirement than the cyclic alkoxy moiety.

L9 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2002 ACS

2001:408051 Document No. 135:19658 Preparation of sildenafil analogs for treatment of erectile dysfunction. Badwan, Adnan Ali H.; El Abadelah, Mustafa M. M. (The Jordanian Pharmaceutical Manufacturing and Medical Equipment Co., Ltd., Jordan). U.S. US 6242444 B1 20010605, 10 pp. (English). CODEN: USXXAM. APPLICATION: US 1999-325876 19990604.

GI



I

AB Title compds. [(un)substituted I; R = (un)substituted pyrrolidino, -piperidino, -morpholino, etc.; R1R2 = (un)substituted CH:N, N:CH, CH:CH, etc.; R3 = H, alkyl, alkanoyl, etc.; Z, Z1 = (un)substituted Cm (sic), O, (alkyl)imino, etc.; m = 1-3] were prepd. Thus, 2,3-dihydrobenzofuran-7-carboxylic acid was amidated by 4-amino-1-methyl-3-propylpyrazole-5-carboxamide and the cyclized product converted in 2 addnl. steps to I (R = 4-methyl-1-piperazinyl, R1R2 = N:CPr, R3 = Me, Z = CH2, Z1 = O). Data for

biol. activity of the prepd. I were given.

L9 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2002 ACS

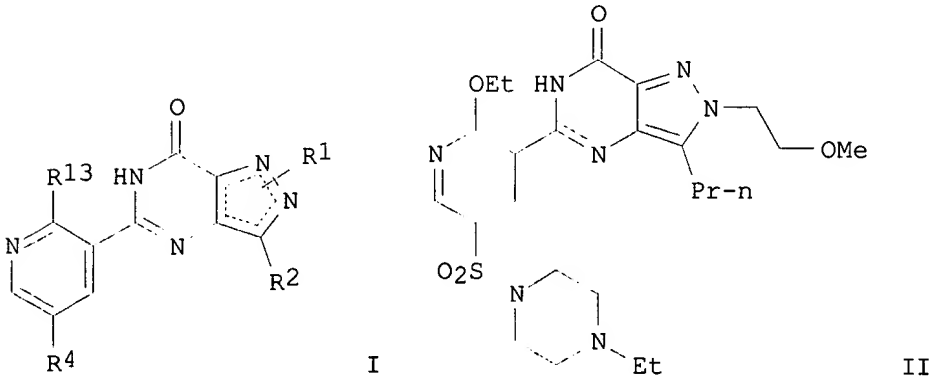
2001:373648 Document No. 135:322800 Determinaton of sildenafil citrate and related substances in the commercial products and tablet dosage form using HPLC. Daraghmeh, N.; Al-Omari, M.; Badwan, A. A.; Jaber, A. M. Y. (The Jordanian Pharmaceutical Manufacturing and Medical Equipment Co. Ltd, Naor, 11710, Jordan). J. Pharm. Biomed. Anal., 25(3-4), 483-492 (English) 2001. CODEN: JPBADA. ISSN: 0731-7085. Publisher: Elsevier Science B.V..

AB This study aimed at developing and validating a HPLC method for the detn. of sildenafil citrate and its related substances that might coexist in the drug com. products and in tablets as impurities that originate from synthesis processes or degrdn. A chromatog. system comprising a .mu.Bondapak C18 (10 .mu.m) column, a mobile phase of pH 7.0 0.2M NH4OAc-MeCN (1:1), a flow rate of 1 mL/min and a UV detector set at 240 nm showed good chromatog. sepn. for sildenafil and other related substances. The degree of linearity of the calibration curves, the percent recoveries of sildenafil and related substances, the limit of detection, LOD, and limit of quantitation, LOQ for the HPLC method were detd. The HPLC method under study was specific, precise, accurate, reproducible indicating stability and robust.

L9 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2002 ACS

2001:283955 Document No. 134:295836 Preparation of 5-(3-pyridyl)-substituted pyrazolo[4,3-d]pyrimidinones as phosphodiesterase inhibitors. Bunnage, Mark Edward; Devries, Keith Michael; Harris, Laurence James; Levett, Philip Charles; Mathias, John Paul; Negri, Joanna Teresa; Street, Stephen Derek Albert; Wood, Albert Shaw (Pfizer Limited, UK; Pfizer Inc.). PCT Int. Appl. WO 2001027113 A2 20010419, 262 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-IB1457 20001011. PRIORITY: GB 1999-24063 19991011; GB 2000-18656 20000728.

GI



AB The title compds. [I; R1 = alkyl, alkenyl, cycloalkyl, etc.; R2 = alkyl, alkenyl, etc.; R13 = OR3, NR5R6 (wherein R3 = alkyl, cycloalkyl, etc.; R5,

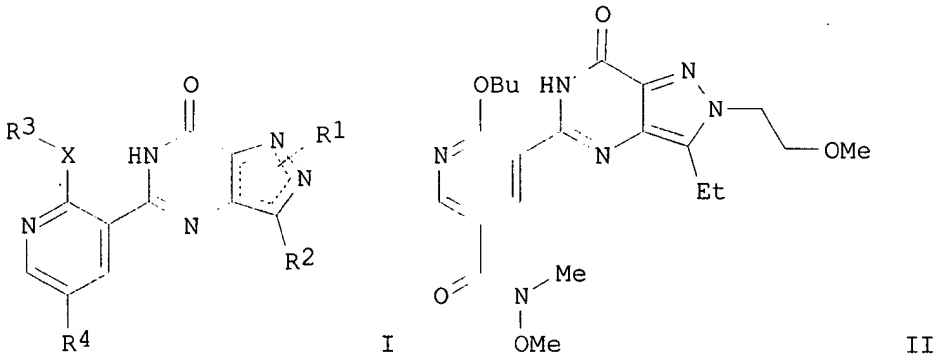
Searched by: Mary Hale 308-4258 CM-1 12D16

R6 = H, alkyl; NR5R6 = azetidino, pyrrolidino, etc.); R4 = substituted at 4-position piperazin-1-ylsulfonyl] and their pharmaceutically or veterinarily acceptable salts which are potent and selective inhibitors of type 5 cyclic guanosine 3',5'-monophosphate phosphodiesterase (cGMP PDE5) and have utility in the treatment of, inter alia, male erectile dysfunction (MED) and female sexual dysfunction (FSD), were prepd. and formulated. E.g., a multi-step synthesis of the pyrazolo[4,3-d]pyrimidinone II which showed IC50 of 2-5 nM against PDE5, was given.

L9 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2002 ACS

2001:283954 Document No. 134:311220 Preparation of pyrazolo[4,3-d]pyrimidin-7-ones as phosphodiesterase inhibitors. Allerton, Charlotte Moira Norfor; Barber, Christopher Gordon; Maw, Graham Nigel; Rawson, David James (Pfizer Limited, UK; Pfizer, Inc.). PCT Int. Appl. WO 2001027112 A1 20010419, 204 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-IB1430 20001004. PRIORITY: GB 1999-24041 19991011; GB 2000-18660 20000728.

GI



I II

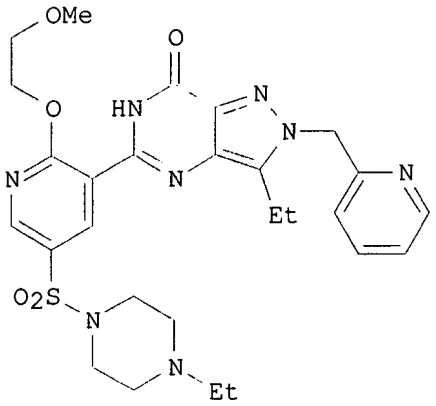
AB The title compds. [I; X = O, NR5; R1 = H, alkyl, Het, etc.; R2 = H, halo, CN, etc.; R3 = H, alkyl, alkylHet, etc.; R4 = H, halo, CN, etc.; R5 = H, alkyl], useful in the curative and prophylactic treatment of a medical condition for which inhibition of a cyclic guanosine 3',5'-monophosphate phosphodiesterase (e.g. cGMP PDE5) is desired such as male erectile dysfunction, were prepd. and formulated. E.g., a multi-step synthesis of the pyrazolo[4,3-d]pyrimidin-7-one II which showed IC50 of 8.5 nM against cGMP PDE5, was given. The compds. I were found to have in vitro activities as inhibitors of cGMP PDE5 with IC50 of < about 100 nM.

L9 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2002 ACS

2001:283943 Document No. 134:295824 Preparation of 3-ethyl-5-[5-(4-ethylpiperazin-1-ylsulfonyl)-2-(2-methoxyethoxy)pyridin-3-yl]-2-(pyridin-2-yl)methyl-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one p-toluenesulfonate. Hughes, Michael Leslie; Storey, Richard Anthony (Pfizer Limited, UK; Pfizer Inc.). PCT Int. Appl. WO 2001027101 A2 20010419, 26 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-IB1445 20001006. PRIORITY: GB 1999-23968 19991011.

GI



I

AB The title compd. I.p-TsOH, useful in treating male erectile dysfunction (no data), was prepd. and formulated. Detailed, multi-step synthesis of I.p-TsOH was given.

L9 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:279456 Document No. 134:295832 Process for the preparation of 1-[5-(7-oxo-2H-pyrazolo[4,3-d]pyrimidin-5-yl)-3-pyridylsulphonyl]piperazines. Devries, Keith Michael; Levett, Philip Charles; Negri, Joanna Teresa; Wood, Albert Shaw (Pfizer Limited, UK; Pfizer Inc.). Eur. Pat. Appl. EP 1092720 A2 20010418, 31 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-308915 20001010. PRIORITY: GB 1999-24042 19991011; GB 2000-18667 20000728.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

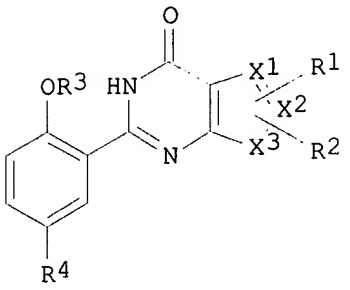
AB The title compds. [I; R = (un)substituted alkyl, cycloalkyl, etc.; R1 = alkyl optionally substituted with Ph, piperidinyl, etc.; R2 = alkyl; NR3R4 = (un)substituted 4-R8-piperazinyl; R8 = H, alkyl, etc.], were prepd. by reacting a compd. II, III or IV [X = a leaving group] in the presence of -OR and a hydroxide trapping agent or in the case of compds. IV reacting in the presence of an auxiliary base and a hydroxide trapping agent (i.e. -OR is substituted by the auxiliary base). E.g., a multi-step synthesis of the pyrazolo[4,3-d]pyrimidinone V was given.

L9 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2002 ACS
2001:179819 Document No. 134:222726 Preparation of phenyl purinone derivatives for the treatment of precancerous lesions. Piazza, Gary A.; Pamukcu, Rifat (Cell Pathways, Inc., USA). U.S. US 6200980 B1 20010313,

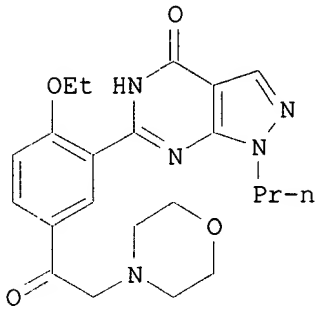
Searched by: Mary Hale 308-4258 CM-1 12D16

31 pp., Cont. of U. S. Ser. No. 472,804. (English). CODEN: USXXAM.
APPLICATION: US 1997-842854 19970417. PRIORITY: US 1995-472804 19950607.

GI



I



II

AB Title compds. (I) [wherein R1 = H, (fluoro)alkyl, or cycloalkyl; R2 = H, (fluoro)alkyl, or cycloalkylalkyl; R3 = (fluoro)alkyl, cycloalkyl(alkyl), alkenyl or alkynyl; R4 = halo or (un)substituted alkyl, alkenyl, alkanoyl, carbamoyl, carboxy, amino, sulfamoylamino, Ph, pyridyl, or imidazoyl, etc.; X1-X3 = independently N or C with the proviso that at least 2 of X1-X3 = N] were prepd. for inhibiting the growth of neoplastic cells. For example, the 4H-pyrazolo[3,4-d]pyrimidin-4-one (II) was formed in a multi-step synthesis involving amidation of 5-amino-1-propylpyrazole-4-carboxamide with 2-ethoxybenzoyl chloride (74%), cyclization using aq. NaOH (89%), acetylation with bromoacetyl bromide in the presence of AlCl3 (92%), and addn. of morpholine in K2CO3 and MeCN (85%). In a cell growth inhibition assay examg. the effects of I on human colon carcinoma cells, administration of 40 .mu.M of 2-(2-propoxyphenyl)-8-azapurin-6-one resulted in 30% apoptotic cells and 2% necrosis compared to 7% and 5%, resp., for the control. Pharmaceutical compns. for oral and parenteral administration of I are also included.

L9 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2002 ACS

2001:133662 Document No. 134:180303 Improved process for preparing pyrazolopyrimidinone derivatives. Chaudhari, Deoram Totaram; Deshpande, Pandurang Balwantrao; Khan, Rashid Abdul Rehman (Orchid Chemicals & Pharmaceuticals Ltd., India). Eur. Pat. Appl. EP 1077214 A1 20010221, 11 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1999-116030 19990816.

AB An improved process for the prepn. of 5-[2-ethoxy-5-(4-methylpiperazin-1-ylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazole[4,3-d]pyrimidin-7-one, which allows to obtain the desired product in good yield and high purity degree, is described.

L9 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2002 ACS

2001:50436 Document No. 134:95497 Phosphodiesterase-inhibiting pyrazolopyrimidinone derivatives conjugated to thiophene moieties or benzo [fused] 5-membered heterocycles for treatment of erectile dysfunction and other cardiovascular disorders. Abdel-Jalil, Raid; Al-Abed, Yousef; El-Abadelah, Mustafa M.; Khanfar, Monther; Sabri, Salim S.; Voelter, Wolfgang (The Picower Institute for Medical Research, USA). PCT Int. Appl. WO 2001003644 A2 20010118, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,

Searched by: Mary Hale 308-4258 CM-1 12D16

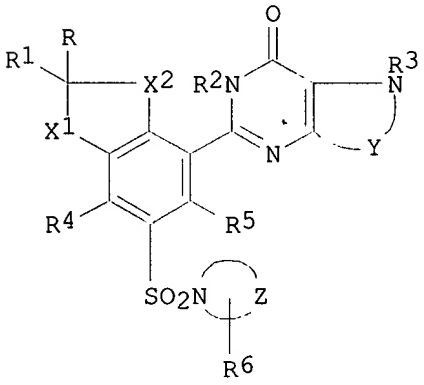
MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US18751 20000707. PRIORITY: US 1999-PV143099 19990709; US 1999-PV149389 19990817.

AB The invention discloses a genus of substituted pyrazolopyrimidinones characterized, in part, by multiply substituted thiophene moieties and, in part, a genus of substituted bicyclic heteroaryl appendages. The compds. are potent inhibitors of phosphodiesterases, particularly cyclic guanosine 3',5'-monophosphate phosphodiesterase activity and are useful for a variety of cardiovascular disorders relating to vascular patency, such as erectile dysfunction. Specifically, a selected set of [benzo]-fused heterocycles includes benzofuran, benzoazole, benzo[d]isoxazole, their 2,3-dihydro analogs, and benzo-1,3-dioxole moieties.

L9 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2002 ACS

2000:865189 Document No. 134:17499 Preparation of pyrazoloppyrimidinone derivatives useful for treatment of erectile dysfunction. Badwan, Adnan Ali H.; El-Abadelah, Mustafa M. M. (Jordanian Pharmaceutical Manufacturing and Medical Equipment Co.Ltd., Jordan). Eur. Pat. Appl. EP 1057829 A1 20001206, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1999-850097 19990604.

GI



I

AB The title compds. I [R-R6 are selected form at least one of group of substituents consisting of (a) H, (b) alkyl, hydroxyalkyl, (c) O-alkyl, S-alkyl, N-(alkyl)n (d) F, Cl, Br, etc.; X1, X2 = Cm, O, S, NR10; Y = CR11:N, N:N, etc.; Z taken with the N atom forms a group selected from pyrrolidinyl, morpholinyl, etc.] were prepd. The disclosed compds. are useful for treatment of inter alia erectile dysfunction. E.g., 5-[2,3-dihydro-5-(4-methylpiperazin-1-ylsulfonyl)-7-benzofuryl]-1-methyl-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-7-one (II) was prepd. In biol. studies using male rats, the ED50 of II was lower than that of sildenafil.

L9 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2002 ACS

2000:758131 Document No. 133:281797 Synthesis of sildenafil. Fu, Heliang; Wang, Xiaoyan; Pang, Baohua; Wang, Ning; Ji, Shangzhong (Tianpu Biochemical Pharmaceutical Co., Ltd., Guangdong, Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1246478 A 20000308, 14 pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 1999-109552 19990712.

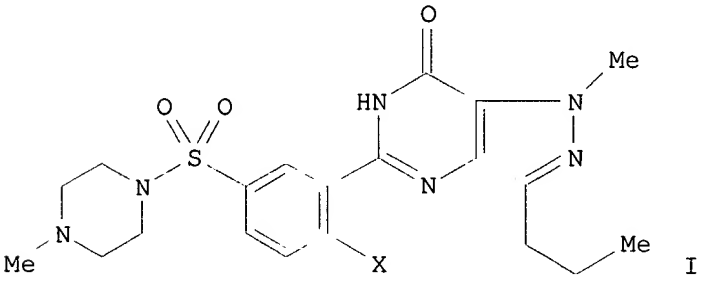
AB The process comprises methylating Et 3-propylpyrazole-5-carboxylate with

di-Me sulfate at 90.degree. for 2.5 h to obtain Et 1-methyl-3-propylpyrazole-5-carboxylate, hydrolyzing with 6M NaOH by refluxing for 3 h to obtain 1-methyl-3-propylpyrazole-5- carboxylic acid, nitrifying with fumed HNO3/fumed H2SO4 at 60.degree. overnight, pouring into ice, filtering to obtain 1-methyl-4-nitro-3-propylpyrazole-5-carboxylic acid, chlorinating with SOCl2. By refluxing for 3 h, acylating with NH4OH to obtain 1-methyl-4-nitro-3-propylpyrazole-5-carboxamide, reducing with SnCl2 2H2O in 95% ethanol by refluxing for 2 h to obtain 4-amino-1-methyl-3- propylpyrazole-5-carboxamide, acylating with 2-ethoxybenzoyl chloride in dichloromethane in the presence of triethylamine and 4- dimethylaminopyridine for 2 h to obtain 4-(2-ethoxybenzamido)-1- methyl-3-propylpyrazole-5-carboxamide, sulfonating with. Chlorosulfonic acid and SOCl2 for 18 h to obtain 4-ethoxy-3-(5- aminocarbonyl-1-methyl-3-propylpyrazol-4-yl)carbamoylbenzenesulfonyl chloride; acylating with piperazine in dichloromethane for 3 h to obtain 1-[4-ethoxy-3-(5-aminocarbonyl-1-methyl-3-propylpyrazol-4-yl)carbamoylbenzenesulfonyl]piperazine, cyclizing in org. solvent in the presence of base and peroxide at 50-170.degree. for 2-72 h to obtain 1-[4-ethoxy-3-(6,7-dihydro-1- methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5- yl)benzenesulfonyl]piperazine, and methylating with CH3I or di-Me sulfate in org. solvent in the presence of formaldehyde and formic acid at 0-120.degree. for 1-48 h.

L9 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2002 ACS

2000:744901 Document No. 133:266864 Preparation of 5-[4-methylpiperazinesulfonylphenyl]-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4.3-d]pyrimidin-7-ones as precursors for preparing sildenafil. Li, Bogang (Diao Pharmaceutical Group Co., Ltd., Chengdu, Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1243832 A 20000209, 7 pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 1999-115009 19990713.

GI



I

AB Title compds. [I; X = F, Cl, Br, I, NO2, NHX1; X1 = CHO, RCO; R = alkyl, cycloalkenyl] are prepd. by acylating 4-amino-1-methyl-3-propylpyrazole-5-carboxamide with 2-XC6H4COCl in dichloromethane in the presence of 4-(N,N-dimethylamino)pyridine and triethylamine at room temp. for 2 h, distg. to recover solvent, extg. with dichloromethane- methanol (19:1) to obtain 4-(2-X-benzamido)-1-methyl-3- propylpyrazole-5-carboxamide; cyclizing in ethanol in the presence of 30% H2O2-NaOH soln. by refluxing for 2.5 h, distg. to recover solvent, adding 10% NaOH soln., extg. with dichloromethane to obtain 5-(2-X-phenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; chlorosulfonating with chlorosulfonic acid at 0.degree. for 14 h under bubbing N2, pouring into ice-water, extg. with dichloromethane to obtain 5-(5- chlorosulfonyl-2-X-phenyl)-1-methyl-3-propyl-1,6-dihydro-7H- pyrazolo[4,3-d]pyrimidin-7-one; acylating with N-methylpiperidine in ethanol at room temp. for 6 h, distg. to recover solvent, extg. with dichloromethane-methanol (9:1), and

recrystg. with methanol-DMF (1:1). Thus, the title compd. I (X = F) was prepd.

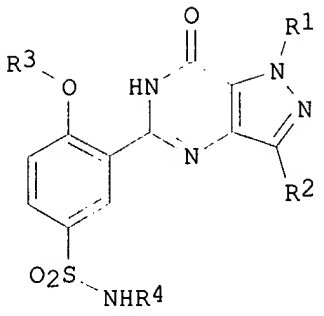
L9 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2002 ACS
2000:595512 Document No. 133:335213 Polymer-supported reagents for multi-step organic synthesis: application to the synthesis of sildenafil. Baxendale, I. R.; Ley, S. V. (Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK). Bioorg. Med. Chem. Lett., 10(17), 1983-1986 (English) 2000. CODEN: BMCLE8. ISSN: 0960-894X. OTHER SOURCES: CASREACT 133:335213. Publisher: Elsevier Science Ltd..
AB Sildenafil, a well known and com. important pharmaceutical drug, has been prepd. using polymer-supported reagents in a multi-step, convergent process resulting in a clean and efficient prepn. without the need for conventional purifn. methods.

L9 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2002 ACS
2000:378770 Document No. 133:17438 Synthesis of sildenafil. Ning, Qi; Zhang, Xiu-Ping (Shanghai Institute of Pharmaceutical Industry, Shanghai, 200437, Peop. Rep. China). Zhongguo Yiyao Gongye Zazhi, 31(4), 145-147 (Chinese) 2000. CODEN: ZYGZEA. ISSN: 1001-8255. Publisher: Zhongguo Yiyao Gongye Zazhi Bianjibu.
AB Sildenafil was synthesized from 2-pentanone in 11 steps. Some reaction conditions had been improved and the total yield raised to 14.2% by using the cheaper reagents.

L9 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2002 ACS
2000:351203 Document No. 132:347588 An improved process for preparing a therapeutically active pyrazolopyrimidinone derivative (sildenafil). Chaudhari, Deoram Totaram; Deshpande, Pandurang Balwantrao; Khan, Rashid Abdul Rehman (Orchid Chemicals & Pharmaceuticals Ltd., India). Eur. Pat. Appl. EP 1002798 A1 20000524, 17 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1998-122031 19981120.
AB The title compd., 5-[2-ethoxy-5-(4-methylpiperazin-1-ylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one, also known with the generic name sildenafil, was prepd. in a few-step synthesis, starting with 1-methyl-4-nitro-3-n-propylpyrazole-5-carboxamide hydrochloride. This improved process provided sildenafil in pure form and very good yield, and further demonstrated to be economically advantageous when compared to the known processes.

L9 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2002 ACS
2000:335412 Document No. 132:334469 Preparation of pyrazolopyrimidinones for the treatment of impotence. Yoo, Moohi; Kim, Wonbae; Chang, Min Sun; Lim, Joong In; Kim, Dong Sung; Kim, Ik Yon; Lim, Tae Kyun; Ahn, Byoung Ok; Kang, Kyung Koo; Son, Miwon; Doh, Hyounmie; Kim, Soonhoe; Shim, Hyunjoo; Oh, Taeyoung; Kim, Heungjae; Kim, Dong Goo (Dong A Pharm. Co., Ltd., S. Korea). PCT Int. Appl. WO 2000027848 A1 20000518, 78 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-KR675 19991110. PRIORITY: KR 1998-48100 19981111; KR 1999-14972 19990427; KR 1999-49384 19991109.
GI

Searched by: Mary Hale 308-4258 CM-1 12D16



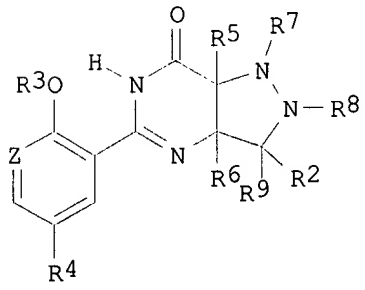
I

AB The title compds. [I; R1 = H, alkyl, fluoroalkyl, cycloalkyl; R2 = H, (un)substituted alkyl, fluoroalkyl, cycloalkyl; R3 = (un)substituted alkyl, fluoroalkyl, cycloalkyl, etc.; R4 = (un)substituted alkyl, alkenyl, cycloalkyl, etc.], useful for the treatment of impotence, one of male sexual dysfunctions, with the side effects reduced, were prepd. E.g., a 3-step synthesis of I [R1 = Me; R2 = Pr; R3 = Et; R4 = iso-Pr] which showed IC50 of 3.74.+-.0.11 ng/mL against PDE 5, was given.

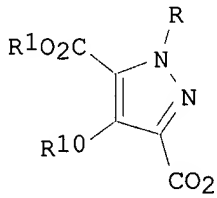
L9 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2002 ACS

2000:291043 Document No. 132:308353 Preparation of pyrazolopyrimidinones as cGMP phosphodiesterase inhibitors. Bunnage, Mark Edward; Maw, Graham Nigel; Rawson, David James; Wood, Anthony; Mathias, John Paul; Street, Stephen Derek Albert (Pfizer Limited, UK; Pfizer Inc.). PCT Int. Appl. WO 2000024745 A1 20000504, 197 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-IB1706 19991019. PRIORITY: GB 1998-23102 19981023; GB 1998-23101 19981023.

GI



I



II

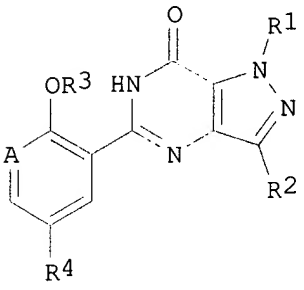
AB Title compds. [I; R2 = CONH2, CO2H, alkoxycarbonyl, (acyl)amino, etc.; R3 = H or (un)substituted alkyl; R4 = SO2NR14R15; R5R6 and R8R9 = bond and R7 = H, alkyl, heterocyclyl, aryl, etc.; R5R7 and R6R9 = bond and R8 = H, alkyl, heterocyclyl, aryl, etc.; NR14R15 = heterocyclyl; Z = CH or N] were prepd. for treatment of sexual dysfunction. Thus, pyrazole-3,5-dicarboxylic acid was nitrated and the product esterified to give

pyrazolecarboxylate II (R = H, R1 = Me, R10 = NO2) which was N-alkylated by 2-chloromethylpyridine and the reduced product amidated by 2-(PrO)C6H4COCl to give II [R = 2-pyridylmethyl, R1 = Me, R10 = NHCOC6H4(OPr)-2]. The latter was heated with NH3 at 100.degree. to give I (R2 = CONH2, R3 = Pr, R5R6,R8R9 = bond, R7 = 2-pyridylmethyl)(III; R4 = H) which was converted to III (R4 = 4-methyl-1-pyrazinylsulfonyl). Data for biol. activity of I were given.

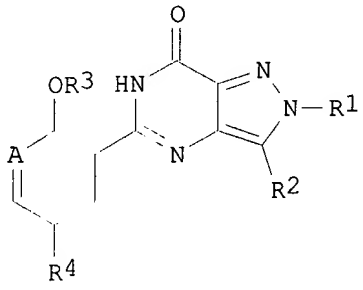
L9 ANSWER 28 OF 41 CAPLUS COPYRIGHT 2002 ACS

2000:277700 Document No. 132:293774 Preparation of pyrazolopyrimidinones as cGMP PDE5 inhibitors for the treatment of sexual dysfunction. Wood, Anthony (Pfizer Inc., USA; Pfizer Limited). Eur. Pat. Appl. EP 995750 A1 20000426, 45 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1999-308156 19991015. PRIORITY: GB 1998-23101 19981023.

GI



I



II

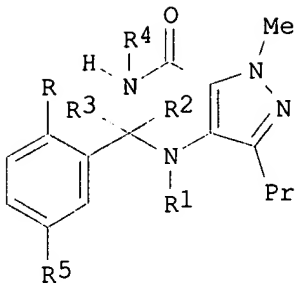
AB The title compds. [I or II; A = CH, N; R1 = (un)substituted Het1, alkylHet1, aryl, etc.; R2, R3 = H, (un)substituted alkyl; R4 = SO2NR12R13; R12, R13 = H, (un)substituted alkyl, Het1, etc.; Het1 = 4-12 membered heterocyclic group contg. at least one N atom and, optionally, one or more heteroatoms selected from N, O and S], useful in the curative and prophylactic treatment of a medical condition for which inhibition of a cyclic guanosine 3',5'-monophosphate phosphodiesterase (e.g. cGMP PDE5) is desired, were prepd. E.g., a multi-step synthesis of II [A = CH; R1 = 2-pyridylmethyl; R2, R3 = Pr; R4 = SO2NMe2] was given. Compds. I and II were found to have in vitro activities as inhibitors of cGMP PDE5 with IC50 of < 100 nM.

L9 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2002 ACS

2000:259773 Document No. 132:279229 Preparation of pyrazolo[4,3-d]pyrimidin-7-ones. Dunn, Peter James; Levett, Philip Charles (Pfizer Limited, UK; Pfizer Research and Development Company, N.V./S.A.). Eur. Pat. Appl. EP 994115 A2 20000419, 20 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1999-307996 19991011. PRIORITY: GB 1998-22238 19981012.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



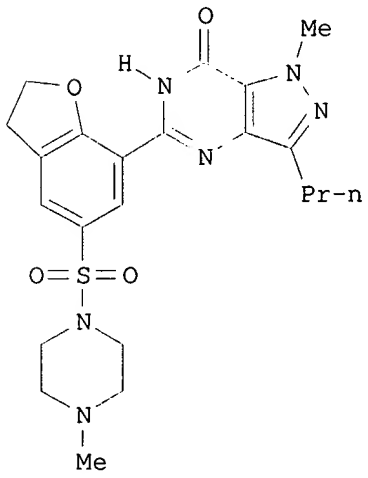
I

AB Title compds. (I; R5 = e.g., 4-methyl-1-piperazinylsulfonyl)(II; R = e.g., OEt; R1R2,R3R4 = bond)(sildenafil) were prepd. in a 1-pot reaction of II (R = leaving group, R1= R4 = H, R2R3 = O) with ethoxide.

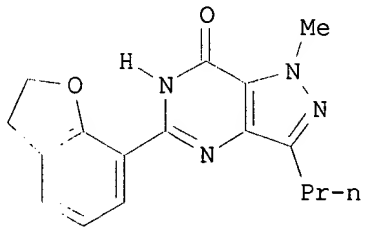
L9 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2002 ACS

1999:793009 Document No. 132:180536 Synthesis and properties of Biagra. A 5-(2,3-dihydro-7-benzofuryl) analog of Viagra. Voelter, Wolfgang; El-Abadelah, Mustafa M.; Sabri, Salim S.; Khanfar, Monther A. (Abtielung fur Physikalische Biochemie, Physiologisch-chemisches Institut der Universitat Tubingen, Tubingen, D-72076, Germany). Z. Naturforsch., B: Chem. Sci., 54(11), 1469-1473 (English) 1999. CODEN: ZNBSEN. ISSN: 0932-0776. OTHER SOURCES: CASREACT 132:180536. Publisher: Verlag der Zeitschrift fuer Naturforschung.

GI



I



II

AB The synthesis and spectral properties (IR, MS NMR) of a substituted 5-(2,3-dihydro-7-benzofuryl)pyrazolo[4,3-d]pyrimidin-7-one I, an analog of Viagra, are described. The generally applicable route involves interaction of 2,3-dihydro-7-benzofuranoyl chloride with 4-amino-1-methyl-3-propyl-5-pyrazolecarboxamide, and the resulting bis-amide is cyclized to the corresponding substituted pyrazolo[4,3-d]pyrimidin-7-one II. Chlorosulfonylation of II followed by treatment with 1-methylpiperazine, furnished the title compd. I (named Biagra). Preliminary expts. "assocd. with the erectile process" on rats lend evidence of greater potency of Biagra as compared to Viagra.

L9 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 12D16

1999:784593 Document No. 132:109700 The Chemical Development of the Commercial Route to Sildenafil: A Case History. Dale, David J.; Dunn, Peter J.; Golightly, Clare; Hughes, Michael L.; Levett, Philip C.; Pearce, Andrew K.; Searle, Patricia M.; Ward, Gordon; Wood, Albert S. (Department of Process Research and Development, Pfizer Central Research Laboratories, Sandwich Kent, CT13 9NJ, UK). Org. Process Res. Dev., 4(1), 17-22 (English) 2000. CODEN: OPRDFK. ISSN: 1083-6160. Publisher: American Chemical Society.

AB The case history of the chem. development of Sildenafil is outlined, covering various aspects of work in chem. development namely: route selection, scale-up issues, the development of an efficient synthesis with high throughput, process safety, and environmental issues. Interesting chem. points include improved methods of prepg. pyrazolo[4,3-d]pyrimidines and the unusual isolation of an intermediate as its double salt (10). The potential dangers of nitrating pyrazole-5-carboxylic acids which are activated to a decarboxylation reaction are discussed.

L9 ANSWER 32 OF 41 CAPLUS COPYRIGHT 2002 ACS

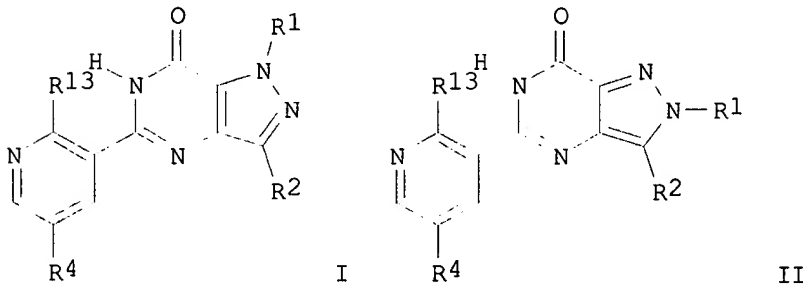
1999:729792 Document No. 132:279187 Synthesis of sildenafil. Shen, Jing; You, Congchao; Wu, Song (Institute of Materia Medica, Chinese Academy of Materia Medica and Peking Union Medical College, Beijing, 100050, Peop. Rep. China). Zhongguo Yaowu Huaxue Zazhi, 9(3), 220-222 (Chinese) 1999. CODEN: ZYHZEF. ISSN: 1005-0108. Publisher: Zhongguo Yaowu Huaxue Zazhi Bianjibu.

AB Sildenafil as new phosphodiesterase V inhibitor was synthesized by a new synthesis route with the total yield of 27.3%.

L9 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2002 ACS

1999:691100 Document No. 131:310644 Preparation of pyrazolopyrimidinone cGMP PDE5 inhibitors for the treatment of sexual dysfunction. Bunnage, Mark Edward; Mathias, John Paul; Street, Stephen Derek Albert; Wood, Anthony (Pfizer Inc., USA; Pfizer Limited). PCT Int. Appl. WO 9954333 A1 19991028, 221 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-IB519 19990325. PRIORITY: GB 1998-8315 19980420; GB 1998-14187 19980630.

GI



I II

AB The title compds. [I or II; R1 = alkyl optionally substituted with (un)substituted Ph, Het or a N-linked heterocyclic group selected from piperidinyl and morpholinyl; R2 = alkyl; R13 = OR3, NR5R6; R3 = alkyl,

Searched by: Mary Hale 308-4258 CM-1 12D16

cycloalkyl, tetrahydrofuranyl, etc.; R4 = SO2NR7R8; R5, R6 = H, alkyl; NR5R6 = pyrrolidino, piperidino, etc.; NR7R8 = 4-(un)substituted piperazinyl, etc.], potent and selective inhibitors of type 5 cyclic guanosine 3',5'-monophosphate phosphodiesterase (cGMP PDE5) which have utility in the treatment of male erectile dysfunction (MED) and female sexual dysfunction (FSD), were prepd. Thus, treatment of 4-[2-(2-ethoxyethoxy)-5-(4-ethylpiperazin-1-ylsulfonyl)pyridin-3-ylcarboxamido]-3-n-propyl-2-(pyridin-2-yl)methylpyrazole-5-carboxamide with tBuOK in 3-methylpentan-3-ol afforded 12% II [R1 = (pyridin-2-yl)methyl; R2 = Pr; R13 = 2-ethoxyethoxy; R4 = 4-ethylpiperazin-1-ylsulfonyl] which showed IC50 of 10.1 nM against cGMP PDE5.

L9 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2002 ACS

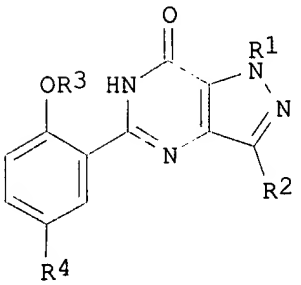
1999:410603 Document No. 131:31948 Processes for preparing sildenafil. Lu, Yee-Fung; Antczak, Casimir; Tao, Yong; Oudenes, Jan (Torcan Chemical Ltd., Can.). Can. Pat. Appl. CA 2235642 AA 19980803, 21 pp. (English). CODEN: CPXXEB. APPLICATION: CA 1998-2235642 19980522.

AB Sildenafil, a known pharmaceutical chem. useful in treatment of male sexual dysfunction, is prepd. by processes in which the final chem. intermediate is of significantly lower basicity than sildenafil itself, so that sildenafil can be extd. in substantially pure form from the org. reaction mixt. in which it is made by adding an aq. medium of appropriately chosen acidic pH and causing phase shift of the sildenafil to occur selectively into the aq. phase.

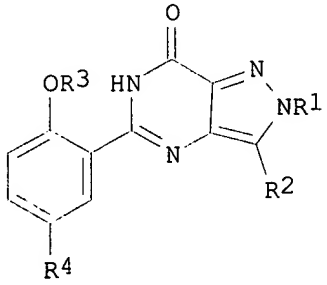
L9 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2002 ACS

1998:721699 Document No. 129:330741 Preparation of pyrazolopyrimidinones as inhibitors of type 5 cyclic guanosine 3',5'-monophosphate phosphodiesterase (cGMP PDE5) for the treatment of sexual dysfunction.. Bunnage, Mark Edward; Mathias, John Paul; Street, Stephen Derek Albert; Wood, Anthony (Pfizer Ltd., UK; Pfizer Inc.). PCT Int. Appl. WO 9849166 A1 19981105, 157 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP2257 19980410. PRIORITY: GB 1997-8406 19970425; GB 1997-15380 19970722; GB 1997-22954 19971030.

GI



I



II

AB Title compds. [I, II; R1 = cycloalkylalkyl, CONR5R6, N-linked heterocyclyl; (CH2)nX; n = 0, 1; X = (substituted) Ph, heterocyclyl; R2 = alkyl; R3 = alkyl, alkoxyalkyl; R4 = SO2NR7R8; R5, R6 = H, alkyl,

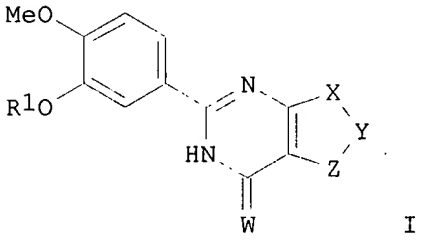
Searched by: Mary Hale 308-4258 CM-1 12D16

alkoxyalkyl; R5R6N = a 5-6 membered heterocyclyl; R7R8N = 4-R10-substituted piperazinyl; R10 = H, (substituted) alkyl], were prepd. as potent and selective cGMP PDE5 inhibitors useful in the treatment of male erectile dysfunction and female sexual dysfunction. Thus, 5-[5-(4-ethylpiperazin-1-ylsulfonyl)-2-propoxyphenyl]-1-(2-morpholin-4-ylethyl)-3-propyl-1,6-dihydro-7H-pyrazolopyrimidin-7-one (prepn. outlined) inhibited cGMP PDE5 with IC50 = 1.9 nM.

L9 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2002 ACS

1998:388524 Document No. 129:54381 Preparation of heterocyclylcatechols as phosphodiesterase inhibitors.. Lee, Jung Geun; Jang, Myung Shik; Shu, Byoung Chul; Lee, Kwang Hyuk; Lee, Yun Ha; Kim, Young Ji (Cheil Jedang Corporation, S. Korea). PCT Int. Appl. WO 9823620 A1 19980604, 25 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-KR150 19970804. PRIORITY: KR 1996-58701 19961128; KR 1997-15476 19970425; KR 1997-27909 19970627.

GI



I

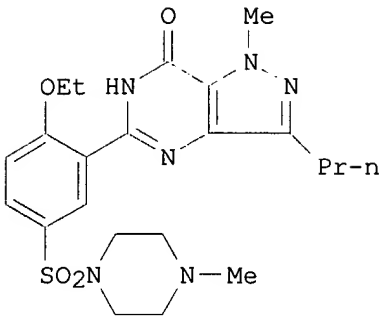
AB Title compds. [I; R1 = alkyl, cycloalkyl, (substituted) Ph, pyrimidyl, pyridyl; X, Y Z = O, N, S optionally substituted with alkyl, cycloalkane, Ph; W = O, S], were prepd. Thus, 4-amino-1H-5-pyrazolecarboxamide in pyridine was treated with 3-cyclopentyloxy-4-methoxybenzoyl chloride (prepn. given) to give 3-(3-cyclopentyloxy-4-methoxybenzoylamino)-1H-pyrazole-4-carboxamide. The latter gave 90% inhibition of phosphodiesterase IV.

L9 ANSWER 37 OF 41 CAPLUS COPYRIGHT 2002 ACS

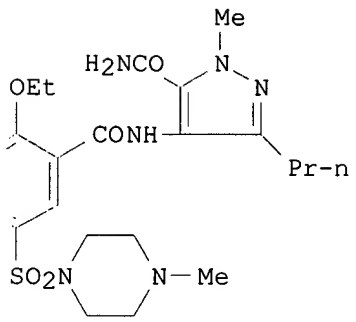
1998:13695 Document No. 128:75412 Process for preparation of Sildenafil by cyclization. Dunn, Peter James; Wood, Albert Shaw (Pfizer Limited, UK; Pfizer Research and Development Company, N.V./s.A.). Eur. Pat. Appl. EP 812845 A1 19971217, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1997-303832 19970604. PRIORITY: GB 1996-12514 19960614.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



I



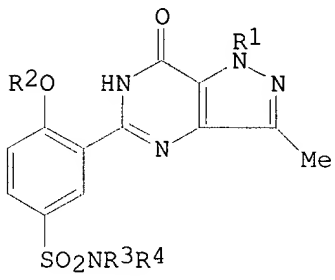
II

AB Sildenfil (5-[2-ethoxy-5-(4-methylpiperazin-1-ylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one, I) is prepd. by cyclization of II under acidic, neutral, or basic conditions. Crude sildenafil product can be obtained of sufficient clin. quality that it may be used for treatment of inter alia (male erectile dysfunction) in humans without further purifn. Prepn. of sildenafil under a broad no. of conditions is given. Thus, II was refluxed in t-BuOH in the presence of potassium tert-butoxide for 8 h. resulting in 90.2% yield of clin. quality I.

L9 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2002 ACS

1993:495547 Document No. 119:95547 Pyrazolopyrimidinone antianginal agents. Brown, David; Terrett, Nicholas Kenneth (Pfizer Ltd., UK; Pfizer Inc.). PCT Int. Appl. WO 9306104 A1 19930401, 26 pp. DESIGNATED STATES: W: CA, FI, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-EP2068 19920904. PRIORITY: GB 1991-19704 19910914.

GI



I

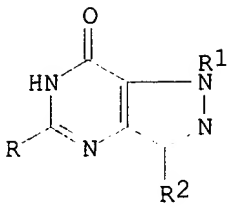
AB Title compds. I (R1 = Me, Et; R2 = Et, Pr; R3, R4 = H, C1-C6 alkyl optionally substituted with C5-C7 cycloalkyl or morpholino), selective cGMP PDE inhibitors useful in the treatment of cardiovascular disorders such as angina, hypertension, heart failure, and atherosclerosis, and their prepn., use, and pharmaceutical compns., are claimed. Synthetic examples and cGMP/cAMP PDE selectivity results are given.

L9 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2002 ACS

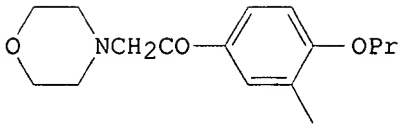
1993:254957 Document No. 118:254957 Preparation of pyrazolopyrimidinones as cGMP phosphodiesterase inhibitors. Bell, Andrew Simon; Terrett, Nicholas Kenneth (Pfizer Ltd., UK; Pfizer Inc.). Eur. Pat. Appl. EP 526004 A1 19930203, 34 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1992-306137 19920702. PRIORITY: GB 1991-14760 19910709.

Searched by: Mary Hale 308-4258 CM-1 12D16

GI



I



AB Title compds. [I; R = 5,2-R4(R3O)C6H3; R1 = H, (cyclo)alkyl, fluoroalkyl; R2 = H, (cycloalkyl)alkyl, fluoroalkyl; R3 = (cyclo)alkyl, fluoroalkyl, alkenyl, etc.; R4 = alkyl, alkenyl, alkanoyl, NH2, halo, Ph, etc.] were prepd. Thus, 4-amino-1-methyl-3-propylpyrazole-5-carboxamide (prepn. given) was N-acylated by 2-(PrO)C6H4COCl and the product cyclized to give I (R1 = Me, R2 = Pr) [II; R = 2-(PrO)C6H4] which was acylated by BrCH2COCl and the product condensed with morpholine to give II (R = morpholinoacetylphenyl group Q) which had IC50 of 1.0 nM against cGMP phosphadiesterase in vitro.

L9 ANSWER 40 OF 41 CAPLUS COPYRIGHT 2002 ACS

1992:255626 Document No. 116:255626 Preparation of pyrazolo[4,3-d]pyrimidin-7-ones as cardiovascular agents. Bell, Andrew Simon; Brown, David; Terrett, Nicholas Kenneth (Pfizer Ltd., UK; Pfizer Inc.). Eur. Pat. Appl. EP 463756 A1 19920102, 26 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1991-305137 19910607. PRIORITY: GB 1990-13750 19900620.

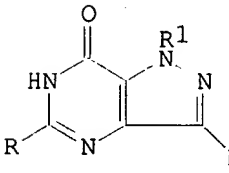
GI For diagram(s), see printed CA Issue.

AB Title compds. [I; R1 = H, (cyclo)alkyl, perfluoroalkyl; R2 = H, (substituted) alkyl, perfluoroalkyl; R3 = alkyl, alkenyl, alkynyl, cycloalkyl, perfluoroalkyl, cycloalkylalkyl; R5 = H, alkyl, alkoxy, amino, aminocarbonyl; X = atoms to complete a pyrrolidinyl, piperidinyl, morpholinyl, or (N-substituted) piperazinyl ring] were prepd. as potent and selective inhibitors of cyclic guanosine 3',5'-monophosphate phosphodiesterase (no data). Thus, 5-(5-chlorosulfonyl-2-ethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (prepn. from Et 3-propylpyrazole-5-carboxylate given) was stirred 4 d with 4-carbamoylpiperidine in EtOH to give title compd. II.

L9 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2002 ACS

1987:50155 Document No. 106:50155 Synthesis and structure-activity relationships of pyrazolo[4,3-d]pyrimidin-7-ones as adenosine receptor antagonists. Hamilton, Harriet W.; Ortwine, Daniel F.; Worth, Donald F.; Bristol, James A. (Dep. Chem., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48105, USA). J. Med. Chem., 30(1), 91-6 (English) 1987. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 106:50155.

GI



I

Searched by: Mary Hale 308-4258 CM-1 12D16

AB A series of 21 1,3-dialkylpyrazolo[4,3-d]pyrimidin-7-ones, e.g., I (R = 2-MeOC6H4, R1 = Me), substituted in the 5-position with various Ph substituents, was prepd. and found to have affinity for the adenosine A1 receptor. The potency pattern due to substituents on the Ph ring was parallel that found in a previously reported (1985) 1,3-dialkyl-8-phenylxanthine series. A quant. structure-activity relationship was developed between these two series that correctly predicted the potencies of six addnl. I. Using the correlation as a guide, I (R = 4-Me2NCH2CH2NSO2C6H4, R1 = Me), having improved aq. soly., was prepd. It is hypothesized that I and analogously substituted xanthines fit the adenosine receptor in an analogous fashion.

=> fil caol;s l3

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	113.10	254.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-25.40	-25.40

FILE 'CAOLD' ENTERED AT 11:16:05 ON 01 FEB 2002

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L10 0 L3

=> del his y